

## PATENT ABSTRACTS OF JAPAN

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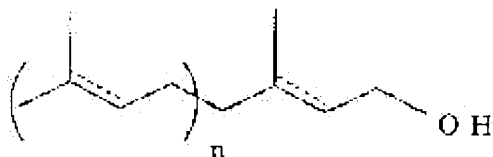
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### (54) COMPOSITION FOR EXTERNAL USE FOR SKIN

(57)Abstract:

PROBLEM TO BE SOLVED: To prepare the subject composition, good in pertucaneous absorptivity or chemical stability, etc., having excellent antiacne properties, hardly causing adverse effects and useful for preventing and treating common acne by including at least one of specific terpene alcohol as an active ingredient therein.

SOLUTION: This composition for external use for skin comprises at least one of 20-25C terpene alcohols, preferably a compound represented by formula I [formula II is a single bond or a bundle bond; (n) is 3 or 4], etc., as an active ingredient. The content of the active ingredient is preferably 0.001-20wt.% and one or more compounds selected from benzoyl peroxide, a macrolide-based antibiotic substance, tetracycline, a carotenoid, etc., are preferably contained therein.



I

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II

LEGAL STATUS

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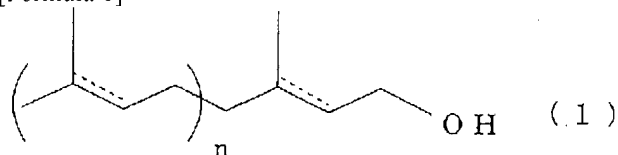
CLAIMS

[Claim(s)]

[Claim 1] simple \*\*\*\* characterized by the number of total carbon containing at least one sort of the terpene alcohol of 20-25 as an active principle -- the skin external use constituent used for prevention and a therapy with that right.

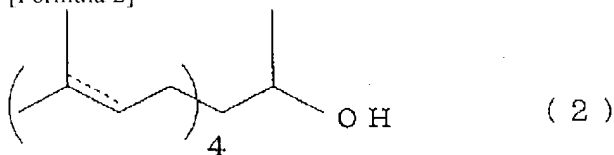
[Claim 2] The skin external use constituent according to claim 1 characterized by terpene alcohol being the compound expressed with following general formula (1) - (4).

[Formula 1]



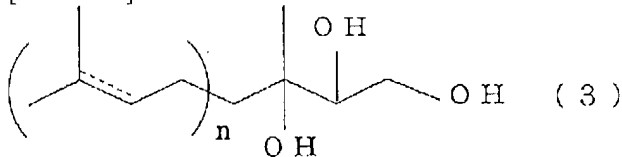
(式中の-----は単結合または二重結合を表し、nは3または4である)

[Formula 2]



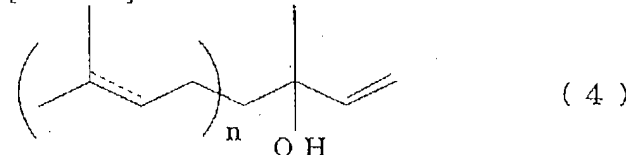
(式中の-----は単結合または二重結合を表す)

[Formula 3]



(式中の-----は単結合または二重結合を表し、nは3または4である)

[Formula 4]



(式中の-----は単結合または二重結合を表し、nは3または4である)

[Claim 3] The skin external use constituent according to claim 1 or 2 characterized by the content of an active principle being 0.001 - 20 % of the weight.

[Claim 4] Furthermore, a skin external use constituent given in any 1 term of claims 1-3 characterized by containing more than a kind of the compound chosen from the group which consists of a benzoyl peroxide, a macrolide, a tetracycline, a carotinoid, a retinoid, sulfur, a salicylic acid, resorcinol, glycyrrhizic acid, and tocopherols.

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## DETAILED DESCRIPTION

[Detailed Description of the Invention]

[0001]

[Field of the Invention] this invention -- the field of cosmetics and skin pharmacology -- setting -- the modulation of the skin -- especially -- simple \*\*\*\* -- it is related with the skin external use constituent used for prevention and a therapy with that right.

[0002]

[Description of the Prior Art] simple \*\*\*\* -- the onset with that right -- the hair follicle -- it is said that cornification of an epithelium, sthenia of sebum secretion, hormone, a bacterial factor, etc. involve. An external use therapy or a general treatment is a core. [ as opposed to these symptoms in the cure in our country ] Although the lotions which are the purposes of keratin exfoliation and contain sulfur or a salicylic acid are widely used about the external use therapy, sufficient effectiveness is not acquired but it is mentioned that it is therefore easy to start prickle fulminant hyperthermia still more multiply. Although tetracyclines or a cephem system antibiotic is used as oral administration about a general treatment, it cannot use to the woman who the administration over a long period of time is required in a serious illness, may show side effects, such as a manifestation of digestive trouble, a hepatopathy, pigmentation, and an exanthema, and has pregnancy and its possibility. moreover, simple \*\*\*\* in the West -- as for the therapy with that right, the oral administration and external use of a vitamin-A-acid derivative, and the external use of a benzoyl peroxide other than an antibiotic are performed. However, the use in our country is not accepted for side effects, such as stimulative [ of both ] or teratogenicity. namely, simple \*\*\*\* -- the present condition is that development of drugs with the safety it is effective and high to the body is demanded to a therapy with that right etc.

[0003]

[Problem(s) to be Solved by the Invention] therefore, simple \*\*\*\* with the safety percutaneous absorption or chemical stability is good, the purpose of this invention has the outstanding anti-\*\* right [ that ] nature, and there are few side effects, and high to the body -- it is in offering the skin external use constituent used for prevention and a therapy with that right.

[0004]

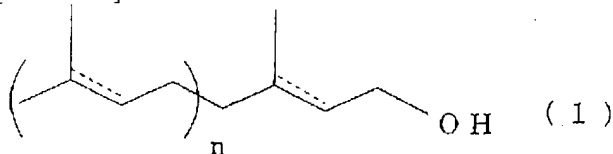
[Means for Solving the Problem] Then, as a result of this invention persons' repeating examination wholeheartedly, the constituent containing a specific compound discovered that the above-mentioned purpose could be attained, and completed this invention. namely, simple \*\*\*\* to which, as for this invention, the number of total carbon is characterized by the thing of the terpene alcohol of 20-25 for which a kind is contained as an active principle at least -- the makeup for the skins or the pharmacology constituent applied to prevention and a therapy with that right is offered.

[0005]

[Embodiment of the Invention] simple \*\*\*\* of the following and this invention -- the skin external use constituent used for prevention and a therapy with that right is explained to a detail. The compound in which the number of total carbon used as an active principle of the skin external use constituent of this invention is shown, for example by following general formula (1) - (4) as terpene alcohol of 20-25 is mentioned.

[0006]

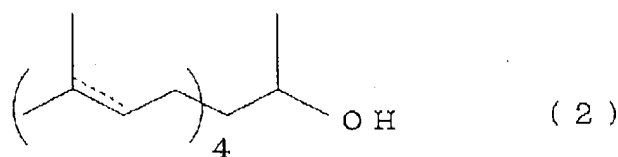
[Formula 5]



(式中の-----は単結合または二重結合を表し、nは3または4である)

[0007]

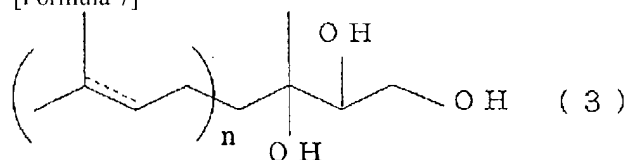
[Formula 6]



(式中の-----は単結合または二重結合を表す)

[0008]

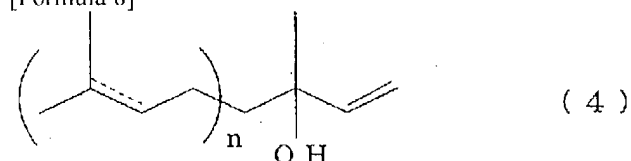
[Formula 7]



(式中の-----は単結合または二重結合を表し、nは3または4である)

[0009]

[Formula 8]



(式中の-----は単結合または二重結合を表し、nは3または4である)

[0010] As an example of a compound expressed with the above-mentioned general formula (1), phytol, a geranyl SAITORO nerol, a geranyl geraniol, a geranyl farnesol, etc. are mentioned. Moreover, as a compound expressed with a general formula (2), iso phytol, geranyl linalool, etc. are mentioned as a compound by which geranyl geranyl isopropanol etc. is expressed with phytantriol etc. and a general formula (4) as a compound expressed with a general formula (3). The terpene alcohol used as an active principle by this invention is not limited to these compounds, and each thing whose numbers of total carbon are 20-25 is usable.

[0011] the content of the above-mentioned active principle in this invention -- simple \*\*\*\* -- although it will not be limited especially if it is sufficient within the limits to do so prevention and a curative effect with that right, it is desirable that it is 0.001 - 20% of the weight of the whole constituent concerned. simple \*\*\*\* with the above-mentioned content sufficient [ less than 0.001% of the weight of a case ] -- when prevention and a curative effect with that right cannot be acquired and 20 % of the weight is exceeded, since stabilization of the constituent concerned may be barred, it is not desirable.

[0012] simple \*\*\*\* of this invention -- since the above-mentioned active principle has the pimple contraction effectiveness, the keratolysis effectiveness, the \*\* right [ that ] curative effect, the hyperkeratosis curative effect, etc., the skin external use constituent used for prevention and a therapy with that right can be suitably used as various cosmetics and a skin external use remedy. To a surprising thing, moreover, the above-mentioned active principle in this invention the prevention to Siwa and a curative effect, and silverfish -- coloring matter, such as - buckwheat dregs, -- self-possessed quenching -- Since it has prevention and the improvement effect of the depressor effect of the anti-inflammation, pigmentation, and scaling in the skin after suntan, and the rough skin, the improvement effect of the dullness in the skin or pore, the effectiveness of preparing the texture of the skin, a whitening operation, etc. It can be suitably used as the part of the skin or the various cosmetics for the whole body, and a skin external use remedy. furthermore, the above-mentioned active principle in this invention -- anti- -- a dandruff -- since it has an operation, the growth promotion effectiveness of the hair, etc., it can be used also as a constituent for the scalp and the hairs.

[0013] simple \*\*\*\* of this invention -- as a use gestalt of the skin external use constituent used for prevention and a therapy with that right, even when it uses as any of cosmetics and a skin external use remedy, the gestalt of a milky lotion, a lotion, a cream, gel, a stick, ointment, a pack, foundation, a skin cleaning agent, etc. can be adopted. simple \*\*\*\* of this invention -- although only the above-mentioned terpene alcohol can be used for the constituent for prevention and a therapy with that right as an active principle also when using as any of cosmetics and a skin external use remedy, it can also blend the component of arbitration suitably according to the use gestalt. As a component of such arbitration, a solvent and an above-mentioned use gestalt usually are embraced, for example. Cosmetics, The thickener currently added and used by the skin chemical, a softener, a superfatting agent, palliative, the component which is damp and is used for \*\*, a surface agent, a preservative, an ultraviolet ray absorbent, a defoaming agent, an oil, a wax, a color or a pigment (simple \*\*\*\* the skin or thing used in order to color the prevention with that right and the therapy agent itself), a preservative and other usual cosmetics, and skin external

preparations is mentioned.

[0014] As the above-mentioned solvent, polyhydric alcohol, such as lower alcohol of the carbon numbers 1-4, such as ethanol and isopropyl alcohol, propylene glycol, and a glycerol, is mentioned, for example. The above-mentioned solvent is suitably blended so that it may exist in the whole constituent concerned at 5 - 99% of the weight of a rate. moreover, simple \*\*\*\* of this invention -- the prevention and the therapy agent with that right use that use gestalt as a milky lotion or a cream -- especially -- desirable -- this time -- said active principle -- in addition, it is desirable to blend the oil (especially silicone system oil); wax of water; fatty alcohol, oxyethylene, poly glycerol fatty alcohol; fatty-acid-ester; nature, or composition etc.

[0015] the case where the constituent of this invention is used as a simple \*\*\*\* right [ that ] remedy -- use gestalten, such as a cream, gel, a lotion, a stick, and ointment, -- it can carry out -- this time -- said active principle -- in addition, in case it considers as these gestalten, the component usually added and blended can be suitably chosen from the components of the above-mentioned arbitration, and can be blended. moreover, the effectiveness can be further heightened by blending one or more sorts, such as macrolides, such as other compounds generally used for a \*\* right [ that ] remedy, for example, a benzoyl peroxide, an erythromycin, clindamycin, and a lincomycin, a tetracycline, a carotinoid, a retinoid, an azurin, sulfur, a salicylic acid, resorcinol, glycyrrhizic acid, a tocopherol, and a female sex hormone.

[0016] the above-mentioned simple \*\*\*\* right [ that ] remedy -- 1 - 3 times of every day, the amount used 0.1 - 2 mg/cm<sup>2</sup> It can be used by continuing to the whole area treated for one week - three months, and applying to it, and, thereby, a good result is obtained. moreover, simple \*\*\*\* of this invention -- also when using the prevention with that right, and a therapy agent as a hyperkeratosis remedy, it can use as the same use gestalt as the case where it uses as the above-mentioned \*\* right [ that ] remedy, and things other than the compound used for the above-mentioned \*\* right [ that ] remedy can also be blended in this case. moreover, the above-mentioned hyperkeratosis remedy can obtain a good result by using it like a \*\*\*\*\* right [ that ] remedy.

[0017]

[Example] the following -- an example -- mentioning -- simple \*\*\*\* of this invention -- although the prevention with that right and a therapy agent are explained further, this invention is not limited to these examples.

(Example of a trial) the pimple contraction effectiveness evaluation trial following trial -- carrying out -- simple \*\*\*\* of this invention -- it evaluated about the pimple (pimple) contraction effectiveness of the compound which is the active principle of the skin external use constituent used for prevention and a therapy with that right. In addition, this pimple contraction effectiveness was histologically evaluated using the hairless RAINO mouse according to the technique of LOWE. Moreover, an exam is 1972VAN. By SCOTT, I am strongly recommended as a model of screening of a pimple remedy.

[0018] The male or the female RAINO mouse (the time of test initiation thing for two months after the birth) was made into five per group, and was distributed to the 1st following group - the 3rd group.

It deals with the 1st group with the ethanol:propylene glycol (7:3) solution (trial matter shown in following [table 1]) of the trial matter.

It deals with the 2nd group with the ethanol:propylene glycol (7:3) solution (quality of contrast shown in following [table 1]) of the quality of contrast.

It deals with the 3rd group with an ethanol:propylene glycol (7:3) solution.

On the back of the RAINO mouse of the one to 3 above-mentioned group, it dealt with the 0.1ml of each above-mentioned solutions by continuation for 13 days (spreading). The skin fragment was extracted from the above-mentioned fragment area with which it dealt on the skin of the back of a RAINO mouse 72 hours after the last treatment. Overnight neglect of this skin fragment was carried out at 4 degrees C into the 0.5-% of the weight acetic-acid solution. Then, after exfoliating the epidermis of a skin fragment from dermis and removing moisture, embedding was carried out to slide glass by suitable embedding agents, and the area of the cross section which becomes the max of the hair follicle was measured with the image analyzer. the following from the obtained measured value -- the formula shown in [a-one number] -- the hair follicle -- it asked for reduction percentage and the pimple contraction effectiveness was evaluated (the hair follicle -- it is shown that there is the pimple contraction effectiveness, i.e., a pimple curative effect, so that reduction percentage is large). Those results are shown in following [table 1].

[0019]

[Equation 1]

$$\text{毛包縮小率(\%)} = 100 - \frac{(\text{化合物塗布群の面ぼう面積})}{(\text{化合物無塗布群(第3群)の面ぼう面積})} \times 100$$

[0020]

[Table 1]

	化 合 物 名	被験濃度 (重量%)	毛包縮小率 (%)
試 験 物 質  (5%)	ゲラニルゲラニオール	5.0	79.4
	ゲラニルリナロール	5.0	24.7
	フィタントリオール	5.0	26.8
	イソフィトール	5.0	32.2
	ゲラニルゲラニルイソプロパノール	5.0	65.4
	フィトール	5.0	44.1
	ゲラニルファルネソール	5.0	68.3
対照	サリチル酸 (10%)	10.0	25.3

[0021] clear from the result of the above [Table 1] -- as -- simple \*\*\*\* of this invention -- the compound which is the active principle of the prevention with that right and a therapy agent showed the pimple contraction effectiveness of having excelled as compared with the salicylic acid.

[0022] The example which prepared various kinds of pharmaceutical preparation with the skin external use constituent of this invention is indicated below.

(Example 1) the anti-\*\* right [ that ] nature cream of the preparation following presentation of an anti-\*\* right [ that ] nature cream was prepared according to the conventional method.

- Geranyl geraniol 1 (% of the weight)  
 - Self-emulsification mold glyceryl monostearate 15 - Palm Oil 8 - Par Hydranalium Squalene 10 - Polyethylene Glycol 400 8  
 - Ethylenediaminetetraacetic Acid 0.05 - Water Residue [0023] (Example 2) the anti-\*\* right [ that ] nature lotion of the preparation following presentation of an anti-\*\* right [ that ] nature lotion was prepared according to the conventional method.

- Geranyl geraniol 1 (% of the weight)  
 - Ethanol 50 - propylene glycol 47.5 - fusibility hydroxypropylcellulose 1.5 [0024] (Example 3) the anti-\*\* right [ that ] nature lotion of the preparation following presentation of an anti-\*\* right [ that ] nature lotion was prepared according to the conventional method.

- Geranyl geraniol 1 (% of the weight)  
 - Ethanol 60 - propylene glycol 10 - glycerol 3 - polyethylene glycol 400 3 - water Residue [0025] (Example 4) the anti-\*\* right [ that ] nature stick of the preparation following presentation of an anti-\*\* right [ that ] nature stick was prepared according to the conventional method.

- Geranyl geraniol 1 (% of the weight)  
 - KARUNABA wax 6 - OZOKERITO 6 - cetyl alcohol 1 - lanolin 6 - antioxidant 0.1 - titanium oxide 20 - yellow and red iron oxide 4.5 - par hydranalium squalene Residue [0026] (Example 5) the anti-\*\* right [ that ] nature cream of the preparation following presentation of an anti-\*\* right [ that ] nature cream was prepared according to the conventional method.

- Geranyl farnesol 1 (% of the weight)  
 - Sulfur 5 - Self-Emulsification Mold Glyceryl Monostearate 15 - Palm Oil 8 - Par Hydranalium Squalene 10 - Polyethylene Glycol 400 8 - Ethylenediaminetetraacetic Acid 0.05 and Water Residue [0027] (Example 6) the anti-\*\* right [ that ] nature lotion of the preparation following presentation of an anti-\*\* right [ that ] nature lotion was prepared according to the conventional method.

- Geranyl farnesol 1 (% of the weight)  
 - Clindamycin 1 - Ethanol 60 - Propylene Glycol 10 - Glycerol 3 - Polyethylene Glycol 400 3 - Water Residue [0028] (Example 7) the anti-\*\* right [ that ] nature ointment of the preparation following presentation of anti-\*\* right [ that ] nature ointment was prepared according to the conventional method.

- Geranyl farnesol 1 (% of the weight)  
 - Vaseline 49 - poly tetrahydrofuran wood ether 49 (viscosity of 22cps) [0029] (Example 8) the anti-\*\* right [ that ] nature stick of the preparation following presentation of an anti-\*\* right [ that ] nature stick was prepared according to the conventional method.

- Geranyl farnesol 2 (% of the weight)  
 - paraffin 30 - paraffin oil 30 - vaseline using it, applying each pharmaceutical preparation of the 38 above-mentioned examples 1-8 to the \*\* right [ that ] affected part one to twice every day, and continuing for one week - three months -- the effectiveness of this invention -- discovered -- simple \*\*\*\* -- it excelled as a skin external use constituent used for prevention and a therapy with that right.

[0030]

[Effect of the Invention] what has the safety percutaneous absorption and chemical stability are good, the skin external use constituent with which the number of total carbon of this invention contains the terpene alcohol of 20-25 as an active principle has the outstanding anti-\*\* right [ that ] nature, and there are few side effects, and high to the body -- it is -- simple \*\*\*\* -- it is suitable as the cosmetics of various gestalten used for prevention and a therapy with that right, and a skin external use remedy.

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[Translation done.]